CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE®

Impact of Malnutrition on Hospitalization Outcomes for Older Adults Admitted for Sepsis

Ashraf Abugroun, MD,[a] Asma Nayyar, MD,[b] Manar Abdel-Rahman, PhD,[c] Pragnesh Patel, MD[d]

[a]Department of Medicine, Medical College of Wisconsin, WI, USA; [b]Departments Internal Medicine, Marshall University Medical Center, WV, USA; [c]College of Health Science-QU Health, Qatar University, Doha, Qatar; [d]Division of Geriatrics, Wayne State University, MI, USA.

ABSTRACT

BACKGROUND: Malnutrition is a major determinant of health outcomes among the older adult population. Our goal was to evaluate the impact of malnutrition on hospitalization outcomes for older adults who were admitted with a diagnosis of sepsis.

METHODS: The National Inpatient Sample was queried for all patients who were admitted with a primary diagnosis of sepsis from January to December 2016. These patients were identified using the International Classification of Diseases, Tenth Revision (ICD-10) diagnosis code A419. Patients who were diagnosed with malnutrition were identified using ICD-10 codes E43, E440, E441, E45, and E46. Outcomes of hospitalization were modeled using logistic regression for binary outcomes and generalized linear models for continuous outcomes.

RESULTS: Overall, a total of 808,030 patients were admitted for sepsis. Those diagnosed with malnutrition were 15.6% (126,335) of the total. The mean age (standard error of the mean) was 78 years (0.03). On multivariate analysis, malnutrition correlated with increased odds for mortality: adjusted OR (aOR) 1.20; 95% confidence interval [CI], 1.15-1.26; $P < .001$; septic shock: aOR 1.50; 95% CI, 1.44-1.57; $P < .001$; and intubation: aOR 1.45; 95% CI, 1.38-1.52; $P < .001$. It was also associated with higher odds for acute kidney injury and stroke. Malnutrition correlated with a 53% increase in the length of stay, with mean ratio 1.53; 95% CI, 1.51-1.56; $P < .01$; and a 54% increase in cost, with mean cost ratio 1.54; 95% CI, 1.51-1.58; $P < .001$.

CONCLUSION: Among the geriatric population diagnosed with sepsis, malnutrition is an independent predictor for poor hospitalization outcomes.

 • The American Journal of Medicine (2021) 134:221−226

KEYWORDS: Geriatrics; Malnutrition; National Inpatient Sample; Sepsis

INTRODUCTION

Malnutrition, according to the American Society of Parenteral and Enteral Nutrition, is defined as an acute, subacute, or chronic state of nutrition in which varying degrees of overnutrition or undernutrition, with or without inflammatory activity, have led to a change in body composition and diminished function.[1] In this context, malnutrition can be attributed to both over- and undernourishment. In our study, malnutrition refers to undernutrition (International Classification of Diseases, Tenth Revision, Clinical Modification [ICD-10-CM] diagnosis codes: E43, E440, E441, E45 and E46) unless stated otherwise. Infections and sepsis, in particular, are detrimental in the geriatric age group and are a huge health care concern owing to its final causative pathway of mortality in the malnourished population, along with elevated morbidity consequences, including deconditioning and debility.[2] It is noted that anthropometric measures of malnutrition are related to the augmented risk and severity of infections caused by numerous pathogenic organisms. Micronutrient and protein caloric deficiency impairs host defense responses with subsequent effects on both innate and adaptive immunity.[3] We analyzed the

Funding: None.
Conflict of Interest: None.
Authorship: All authors had a role in writing the manuscript.

Requests for reprints should be addressed to Ashraf Abugroun, MD, Section of Hospital Medicine / Division of General Internal Medicine-Froedtert & The Medical College of Wisconsin. Phone: (414) 955-0350 / Fax: (414) 955-0094

E-mail address: aabugroun@mcw.edu

0002-9343/© 2020 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.amjmed.2020.06.044

health care utilization burden in terms of mortality, in-hospital complications, length of stay, and hospitalization cost, as most of the time, critical care admission is warranted in malnourished older adults admitted for sepsis.[2]

METHODS

Data Sources

The National (Nationwide) Inpatient Sample (NIS) is the largest publicly available all-payer inpatient care database in the United States. It contains data on more than 7 million hospital stays with a weighted estimate of 35 million hospital stays each year.[4] The NIS contains clinical and nonclinical data elements, including demographics, socioeconomic, diagnosis, and comorbidity measures, in-hospital procedural records, length of stay, and total charges for each hospitalization record. Hospital charges represent the total amount that hospitals billed for services. The Healthcare Cost and Utilization Project cost-to-charge ratios are based on each hospital's accounting reports collected by the Centers for Medicare & Medicaid Services. According to the Healthcare Cost and Utilization Project database, NIS data conform to the definition of limited data set in which 16 direct identifiers have been removed.[5] Accordingly, institutional review board approval was not deemed necessary because NIS uses previously collected publicly available de-identified data.

CLINICAL SIGNIFICANCE

- The prevalence of malnutrition among older patients admitted for sepsis is 15.6%.
- Malnutrition is an independent predictor for increased odds for mortality, septic shock, and need for intubation among older patients admitted for sepsis.
- Malnutrition correlates with a 53% increase in length of stay and 54% increase in cost following admission of older patients for sepsis.

Study Population

The NIS was queried for records of all patients aged ≥65 years who were admitted with a primary diagnosis of sepsis from January to December 2016. These patients were identified using the ICD-10 diagnosis code A419. Patients who were diagnosed with malnutrition were identified using ICD-10 codes E43, E440, E441, E45, and E46. Supplementary Table 1 (available online) summarizes the complete list of ICD codes used in the study.

Study Variables

Study variables included patient's age at the time of admission, sex, race (white, black, and other), household income, the primary payer (private insurance, Medicare, Medicaid, and other [self-pay]), presence or absence of comorbidities as defined by the Elixhauser comorbidity index; hospital characteristics including hospital location and teaching status, hospital bed size (small, medium, and large), and ownership were defined according to the NIS coding.

The primary outcomes in this study were all-cause in-hospital mortality, septic shock, intubation, and mechanical ventilation. Other clinical outcomes included acute kidney injury, myocardial infarction, stroke, length of stay, and total cost as secondary outcomes. The cost was calculated by using charges available in the NIS and multiplied by the accompanying cost-to-charge ratios.

Statistical Analysis

Categorical variables were presented as percentages. Continuous variables with normal distribution are expressed as mean ± standard error of the mean (SEM). Continuous variables that were skewed were expressed as median with interquartile ranges. Given the large population size, the standardized mean-difference effect size (d) was obtained for each variable.

$$d = \frac{100 * (\bar{x}_1 - \bar{x}_2)}{\sqrt{(s_1^2 + s_2^2)/2}},$$

where $\bar{x}_1$ and $\bar{x}_2$ are the sample means for the malnutrition and nonmalnutrition groups, respectively, and s_1^2 and s_2^2 are the respective sample variances.[6] A standardized difference of 0.1 or higher is considered clinically important.[6] The cost for each in-patient hospitalization was measured for each patient by multiplying the total hospital charge with the cost-to-charge ratio provided by the NIS database. Outcomes of hospitalization were modeled using logistic regression for binary outcomes. Cost and length of stay were modeled using generalized linear models with log link and gamma function and negative binomial family, respectively. Potential patient-level factors including demographics, insurance type, and comorbid conditions, as well as hospital-level factors including hospital size, teaching status, and ownership were adjusted in the multivariate analysis. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported for binary outcomes, and incidence rate ratio also referred to as means ratio with 95% CIs for the numeric outcomes. Calculated means ratio represents the increase or decrease in percentage associated with length of stay and cost.[7,8] For example, incidence rate ratio of 1.1 for the length of stay represents a 10% increase in mean length of stay. All analyses were performed using STATA 15 (Stata Corp LLC, College Station, Texas); a P value < .05 was considered significant.

RESULTS

Study Patients

Of the 808,030 older adults with a hospitalization record of sepsis in 2016, 126,335 patients (15.6%) were diagnosed with malnutrition. The mean age (SEM) was 78 years (0.03). The majority of patients were female (52%) and of the white race (76.2%). Among patients admitted for sepsis, 30.8% had pneumonia, 24.6% had a urinary tract infection,

Table 1 Baseline Characteristics of the Study Population

	Control	Malnutrition	Total	Effect Size (*d*)
Unweighted number	136,339	25,267	161,606	
Weighted number	681,695	126,335	808,030	
Females	51.9%	52.4%	52%	0.0
Age, years (Standard error of the mean)	77.9 (0.03)	78.3 (0.06)	78 (0.03)	0.0
Race				0.0
White	77.2%	70.5%	76.2%	Ref
Black	9.4%	14.3%	10.2%	0.2
Hispanic	7.5%	8.1%	7.6%	0.0
Asian or Pacific Islander	3.2%	4.1%	3.3%	0.1
Sepsis etiology				
Pneumonia	31.4%	27.6%	30.8%	0.0
Urinary tract infection	24.6%	24.5%	24.6%	0.0
Pneumonia & urinary tract infection	8.7%	10.9%	9.0%	0.1
Soft tissue infection	5.7%	4.2%	5.4%	0.0
Comorbidities				
Vitamin D deficiency	1.8%	2.4%	1.9%	0.0
Obesity	13.1%	9.9%	12.6%	−0.1
Deficiency anemias	28.8%	41.9%	30.9%	0.3
Autoimmune disease	7.9%	7.9%	7.9%	0.0
Congestive heart failure	30.4%	30.6%	30.4%	0.0
Valvular disease	9.4%	8.0%	9.2%	0.0
Chronic lung disease	42.0%	46.4%	42.7%	0.1
Diabetes mellitus	39.0%	32.1%	37.9%	−0.1
Hypertension	72.5%	65.6%	71.4%	−0.1
Hypothyroidism	19.2%	17.6%	18.9%	0.0
Alcohol abuse	2.2%	3.2%	2.3%	0.1
Drug abuse	1.3%	1.6%	1.3%	0.0
Liver disease	5.7%	7.6%	6.0%	0.1
Chronic kidney disease	29.3%	29.6%	29.3%	0.0
Solid tumors (no Mets)	7.8%	13.4%	8.7%	0.2
Peripheral vascular disease	11.5%	14.0%	11.9%	0.1
Psychoses	2.9%	3.2%	3.0%	0.0
Atrial fibrillation	30.9%	31.0%	31.0%	0.0
Coronary artery disease	29.8%	24.8%	29.0%	−0.1
Hyperlipidemia	40.6%	32.8%	39.4%	−0.2
Tobacco use	0.8%	0.7%	0.8%	0.0
Obstructive sleep apnea	8.7%	4.0%	8.0%	−0.2
Prior Stroke	10.9%	9.7%	10.8%	0.0
Do not resuscitate status	25.8%	33.7%	27.0%	0.2
Elective admission	3.1%	3.4%	3.1%	0.0
Median household income				
0-25th percentile	27.6%	31.7%	28.3%	Ref
26th-50th percentile	26.1%	24.1%	25.8%	0.0
51st-75th percentile	24.9%	23.9%	24.8%	0.0
76th-100th percentile	21.3%	20.3%	21.2%	0.0
Primary expected payer				
Medicare	89.5%	90.3%	89.7%	Ref
Medicaid	1.7%	2.2%	1.8%	0.0
Private insurance	6.6%	5.5%	6.5%	0.0
Self-pay	0.5%	0.5%	0.5%	0.0
Bed size of hospital				
Small	20.6%	19.0%	20.3%	Ref
Medium	31.0%	31.6%	31.1%	0.0
Large	48.4%	49.4%	48.5%	0.0
Location/teaching status of hospital				
Rural	11.4%	8.7%	10.9%	Ref
Urban nonteaching	30.5%	31.3%	30.7%	0.0
Urban teaching	58.1%	60.0%	58.4%	0.0

Table 2 Mortality and Complication Rate Among older Patients Admitted for Sepsis With and Without Malnutrition

	Control	Malnutrition	Total	Effect Size (*d*)
Mortality	12.6%	17.5%	13.4%	0.1
Septic shock	18.7%	28.4%	20.3%	0.2
Intubation	9.9%	15%	10.7%	0.2
AKI	41.5%	49.5%	42.7%	0.2
Acute MI	6%	6.2%	6%	0.0
Stroke	1.6%	2.2%	1.7%	0.1
LOS Days (IQR)	5 (3-8)	7 (4-12)	5 (3-8)	0.6
Cost USD (IQR)	9782 (6010-16,794)	14,786 (8491-27,883)	10,342 (6263-18,209)	0.4

AKI = acute kidney injury; IQR = interquartile range; LOS = length of stay; MI = myocardial infarction; USD = US dollars.

Table 3 Correlation Between Malnutrition and Study Outcomes

	Adjusted OR*	95% CI	*P* Value
Mortality	1.20	1.15-1.26	<.001
Septic shock	1.50	1.44-1.57	<.001
Intubation	1.45	1.38-1.52	<.001
Acute kidney injury	1.33	1.28-1.38	<.001
Myocardial infarction	1.00	0.94-1.07	.99
Stroke	1.24	1.13-1.37	<.001
Cost	1.54	1.51-1.58	<.001
Length of stay	1.53	1.51-1.56	<.001

*Calculated odds ratio was adjusted for age, sex, race, components of Elixhauser comorbidity index, and other comorbidities that had significant association with each outcome at univariate level, insurance type, hospital location, bed-size and teaching status and hospital ownership.
CI = confidence interval; OR = odds ratio.

and 9% had both pneumonia and a urinary tract infection. Those who had skin and soft tissue infection accounted for 5.4% of the total. Overall, patients with malnutrition had a higher prevalence of deficiency anemias, chronic obstructive lung disease, peripheral vascular disease, alcohol abuse, liver disease, and malignancies. Table 1 summarizes the results of the remaining patients' baseline clinical and other characteristics.

Primary Outcomes

Patients with malnutrition had higher rates of mortality (17.5% vs 12.6%), $d = 0.1$; septic shock (28.4% vs 18.7%), $d = 0.2$; and need for intubation (15% vs 9.9%), $d = 0.2$ (Table 2). On multivariate analysis, presence of malnutrition was independently associated with higher odds for mortality, adjusted OR (aOR): 1.20; 95% CI, 1.15-1.26; $P < .001$; septic shock: aOR 1.50; 95% CI, 1.44-1.57; $P < .001$; and intubation: aOR 1.45; 95% CI, 1.38-1.52; $P < .001$ (Table 3).

Secondary Outcomes

Patients with malnutrition had higher rates of acute kidney injury: (49.5 vs 41.5), $d = 0.2$; and stroke: (2.2 vs 1.6), $d = 0.1$; but no significant difference in rates for acute myocardial infarction. Patients with malnutrition had an overall higher length of stay with median (interquartile range [IQR]) 7 (4-12) vs 5 (3-8) days, $d = 0.6$; and higher cost for hospitalization 14,786 (IQR 8491-27,883) vs 9782 (IQR 6010-16,794) USD, $d = 0.4$ (Table 2). On multivariable analysis, malnutrition correlated with higher odds for acute kidney injury: 1.33; 95% CI, 1.28-1.38; $P < .001$; and stroke: 1.24; 95% CI, 1.13-1.37; $P < .001$. Malnutrition correlated with a 53% increase in the length of stay, with means length of stay ratio 1.53; 95% CI, 1.51-1.56; $P < .01$; and a 54% increase in cost, with means cost ratio 1.54; 95% CI, 1.51-1.58; $P < .001$ (Figure 1, Table 3).

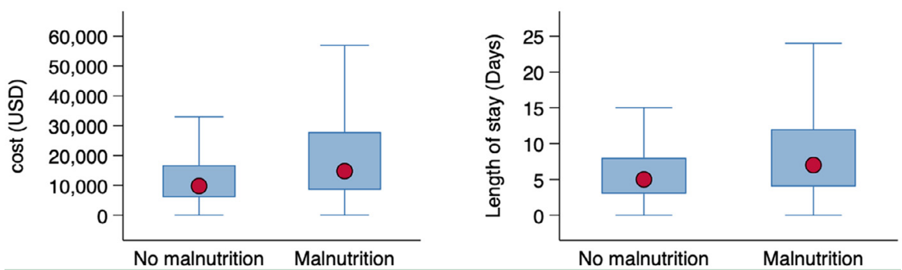

Figure 1 The cost and length of stay in study patients with and without malnutrition.

DISCUSSION

Our study showed that the presence of malnutrition is associated with poor hospitalization outcomes among older adults admitted for sepsis. We performed a multivariable analysis with adjustment for patient demographics, socioeconomic factors along with comorbidities and hospital characteristics, and concluded that malnutrition has an independent association with increased mortality, in-hospital adverse events, prolonged length of stay, and higher hospitalization cost.

According to literature, the prevalence of malnutrition in general hospitals and among the geriatric population ranges from 11% to 44% and 29% to 61%, respectively.[9] This is similar to findings from our study, as 15.6% of older patients who were hospitalized for sepsis were diagnosed with malnutrition. While there is variability in the clinical parameters used to define malnutrition, in this study malnutrition is defined based on ICD-10 billing codes. According to the American Society for Parenteral and Enteral Nutrition, severe malnutrition is diagnosed based on a percentage of energy intake and rate for weight loss, muscle mass, and body fat loss, as well as the presence of edema and reduced grip strength.[10] Grounded on these parameters, patients are labeled with the corresponding ICD-10 codes for malnutrition. Proper assignment of ICD codes is the responsibility of each hospital contributing to the NIS.

Sepsis is considered as one of the most expensive conditions being treated in hospitals across the United States.[11] In addition, sepsis is also associated with a higher readmission rate, which further adds to the economic burden.[12] In the current analysis, sepsis ranked as the most common reason for admission among adults aged ≥65 years (Supplementary Table 2 available online). Sepsis results in intravascular volume depletion along with simultaneous vasodilation, causing an imbalance in oxygen supply and demand in various organ systems. Additionally, sepsis results in the activation of inflammatory cascades, with subsequent potential for coagulopathy mediated by endothelial cell dysfunction.[13,14] Potential synergism between malnutrition and infection is being reported.[15] Malnutrition has an independent association with a higher risk of mortality and risk for adverse events.[16] In addition, malnutrition and muscle wasting from protein loss (sarcopenia) are part of the frailty syndrome and are associated with poor outcomes.[17]

Malnutrition imposes negative outcomes through multiple mechanisms. For instance, malnutrition causes alterations in the systemic regulatory functions and immune suppression. It induces disturbance in homeostasis, causing a limited reserve to combat stressors. It also results in increased permeability of the intestinal epithelial barrier, which facilitates the translocation of gut flora, particularly bacteria.[18] Also, micronutrient and multivitamin deficiencies can independently influence outcomes and increase the risk of complications. For instance, lower level of vitamin D can result in immune dysregulation, defective mucosal function and endothelial dysfunction, which can result in a higher risk of adverse events.[19,20] Moreover, hypoalbuminemia can lead to decreased efficacy of the transport of highly protein-bound antibiotics, hence, a higher proportion of medication ends up being filtered and eliminated in vivo.[21]

Interestingly, 9.9% of older malnourished patients seen in this study were obese. Higher body mass index does not necessarily correlate with the lean muscle mass and can be elevated in conditions that predispose to fluid overload, as in cardiac, renal, and hepatic disorders. Paradoxical malnourishment in obese patients could also be linked to the intake of calorie-rich but protein- and nutrient-poor diet.[9]

Our study presented some limitations; it is based on administrative databases, which may vary in accuracy. The use of ICD codes may have led to underestimation of the diagnoses of certain comorbidities and complications. Laboratory data, including albumin, prealbumin, and micronutrient level, were not included in the database. As this is a cross-sectional observational study, a cause-and-effect relationship between malnutrition and adverse outcomes cannot be ascertained. It is unclear whether malnutrition plays a causative role in adverse outcomes or if it serves as a marker for decreased health status, chronic inflammation, hormonal and metabolic derangements, more advanced comorbidities, or frailty. The adjusted OR for mortality in septic patients attributed to malnutrition is relatively modest and potentially subject to residual confounding not accounted for in the multivariable models. Finally, the study is limited to the in-hospital events, and post-discharge follow-up was not inferred; in addition, due to lack of data on timing of events following hospitalization, it was not possible to obtain competing risk analysis, which would have provided a better estimation of the risk attributed to the presence of malnutrition.

The primary strength of this study is the availability of a large sample from multiple hospitals, centers, and geographic locations that are representative of the entire US population. Strict adherence to the NIS methodological standards was followed.[22] In addition, confounding bias was mitigated by performing a multivariable analysis with adjustment for demographics, comorbidities, socioeconomic factors, insurance type, and hospital characteristics including bed size, teaching status, and hospital ownership, thus minimizing the impact of selection bias.

In conclusion, the association of malnutrition with hospital outcomes related to sepsis is reflected with a spectrum of increased mortality, higher complication rates, longer duration of stay, and a higher cost of hospitalization compared with what it has been otherwise. Particular consideration for early recognition of malnutrition and meticulous efforts for routine surveillance should be done, as malnutrition is highly linked to worse hospitalization outcomes. Additional study is needed to determine if nutritional support can improve outcomes in older adults hospitalized with sepsis and concomitant malnutrition.

References

1. American Society for Parenteral and Enteral Nutrition (ASPEN). Definitions: malnutrition. Available at: https://www.nutritioncare.org/Guidelines_and_Clinical_Resources/Toolkits/Malnutrition_Toolkit/Definitions/. Accessed May 7, 2020.
2. Abd Aziz NAS, Teng NIMF, Abdul Hamid MR, Ismail NH. Assessing the nutritional status of hospitalized elderly. *Clin Interv Aging* 2017;12:1615–25.
3. Ibrahim MK, Zambruni M, Melby CL, Melby PC. Impact of childhood malnutrition on host defense and infection. *Clin Microbiol Rev* 2017;30(4):919–71.
4. Healthcare Cost and Utilization Prject (HCUP). NIS description of data elements. Available at: https://www.hcup-us.ahrq.gov/db/nation/nis/nisdde.jsp. Accessed December 9, 2019.
5. Healthcare Cost and Utilization Prject (HCUP). DUA training – accessible version. Available at: https://www.hcup-us.ahrq.gov/DUA/dua_508/DUA508version.jsp. Accessed February 13, 2020.
6. Grissom R, Kim JJ. *Effect Sizes for Research: Univariate and Multivariate Applications*. 2nd ed New York: Routledge, Taylor & Francis Group; 2012.
7. Kumar AJ, Henzer T, Rodday AM, Parsons SK. Risk factors for length of stay and charge per day differ between older and younger hospitalized patients with AML. *Cancer Med* 2018;7(6):2744–52.
8. Adejumo AC, Akanbi O, Pani L. Among inpatients, ischemic bowel disease predisposes to *Clostridium difficile* infection with concomitant higher mortality and worse outcomes. *Eur J Gastroenterol Hepatol* 2019;31(1):109–15.
9. Yi PH, Frank RM, Vann E, Sonn KA, Moric M, Della Valle CJ. Is potential malnutrition associated with septic failure and acute infection after revision total joint arthroplasty? *Clin Orthop* 2015;473(1):175–82.
10. Association of Clinical Documentation Integrity Specialists (ACDIS). Q&A: documentation and ICD-10-CM coding for severe malnutrition | ACDIS. Available at: https://acdis.org/articles/qa-documentation-and-icd-10-cm-coding-severe-malnutrition. Accessed November 28, 2019.
11. Paoli CJ, Reynolds MA, Sinha M, Gitlin M, Crouser E. Epidemiology and costs of sepsis in the United States—an analysis based on timing of diagnosis and severity level. *Crit Care Med* 2018;46(12):1889–97.
12. Mangels AR. CE: malnutrition in older adults. *Am J Nurs* 2018;118(3):34–41.
13. Shao IY, Elkind MSV, Boehme AK. Risk factors for stroke in patients with sepsis and bloodstream infections. *Stroke* 2019;50(5):1046–51.
14. Kakihana Y, Ito T, Nakahara M, Yamaguchi K, Yasuda T. Sepsis-induced myocardial dysfunction: pathophysiology and management. *J Intensive Care* 2016;4(1):22.
15. Katona P, Katona-Apte J. The interaction between nutrition and infection. *Clin Infect Dis* 2008;46(10):1582–8.
16. Farhadi S, Ovchinnikov RS. The relationship between nutrition and infectious diseases: a review. *BBRJ* 2018;2(3):108–72. https://doi.org/10.4103/bbrj.bbrj_69_18. Accessed February 12, 2020.
17. Sieber CC. Malnutrition and sarcopenia. *Aging Clin Exp Res* 2019;31(6):793–8.
18. de Souza Menezes F, Leite HP, Koch Nogueira PC. Malnutrition as an independent predictor of clinical outcome in critically ill children. *Nutrition* 2012;28(3):267–70.
19. Upala S, Sanguankeo A, Permpalung N. Significant association between vitamin D deficiency and sepsis: a systematic review and meta-analysis. *BMC Anesthesiol* 2015;15:84.
20. De Pascale G, Vallecoccia MS, Schiattarella A, et al. Clinical and microbiological outcome in septic patients with extremely low 25-hydroxyvitamin D levels at initiation of critical care. *Clin Microbiol Infect* 2016;22(5):456.e7–456.e13.
21. Arnau-Barrés I, Güerri-Fernández R, Luque S, Sorli L, Vázquez O, Miralles R. Serum albumin is a strong predictor of sepsis outcome in elderly patients. *Eur J Clin Microbiol Infect Dis* 2019;38(4):743–6.
22. Khera R, Krumholz HM. With great power comes great responsibility: big data research from the National Inpatient Sample. *Circ Cardiovasc Qual Outcomes* 2017;10(7):e003846.

SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjmed.2020.06.044.

Supplementary Table 1 ICD-10 Codes Used for Defining Study Variables

	ICD-10 Codes
Sepsis	A419
Malnutrition	E43 E440 E441 E45 E46
Pneumonia	A0103 A0222 A3701 A3711 A3781 A3791 A5484 B012 B052 B0681 B7781 J09 × 1 J1000 J1001 J1008 J1100 J1108 J1281 J1289 J129 J13 J14 J150 J151 J1520 J15211 J15212 J1529 J153 J154 J155 J156 J157 J158 J159 J160 J168 J17 J180 J181 J182 J188 J189 J851 J95851 J120 J121 J122 J123
Urinary tract infection	N390 N10 N300*
Skin and soft tissue infection	L02* L03*
Intubation	0BH17EZ 0BH18EZ 5A1935Z 5A0945Z
DNI status	Z66
Septic shock	R6521 T8112XA T8112XS A483
Myocardial infarction	I2101 I2102 I2109 I2111 I2119 I2121 I2129 I213 I214
Acute kidney injury	N170 N171 N172 N178 N179
Acute stroke	I60* I61* I62* I63*

DNI = do not intubate; ICD-10 = International Classification of Diseases, Tenth Revision.

Supplementary Table 2 Top 10 Diagnoses for Admission for Patients Aged >65 Years During the Year 2016 from the National Inpatient Sample

Rank	ICD-10 Code	Diagnosis	Number
1	A419	Sepsis	808,029
2	J189	Pneumonia	355,909
3	N179	AKI	307,604
4	J441	COPD	295,804
5	I214	NSTEMI	289,139
6	N390	UTI	255,549
7	I5033	Acute on chronic diastolic heart failure	187,444
8	I639	Cerebral infarction	172,369
9	M1711	Osteoarthritis of the knee	171,565
10	I5023	Acute on chronic systolic heart failure	159,929

AKI = acute kidney injury; COPD = chronic obstructive pulmonary disease; ICD-10 = International Classification of Diseases, Tenth Revision; NSTEMI = non-ST-elevation myocardial infarction; UTI = urinary tract infection.